REMARKS

Claims 8 to 11, 46, and 68 to 98 are pending in the present application. Claims 8, 46, 69, 74, 76, 78, 84 to 86 and 90 to 92 have been canceled herein without prejudice to Applicants pursuing these claims in one or more applications that claim the benefit of priority to the present application. Claims 9, 11, 68, 70 to 72, and 75 have been amended herein. Thus, upon entry of the present amendments, claims 9 to 11, 68, 70 to 72, 75, 77, 79 to 83, 87 to 89, and 93 to 98 will be under examination. Claims 9, 10, 77 to 82, 84 and 85 were indicated to be allowable in the Office Action mailed November 20, 2003.

Regarding the amendments

Claims 9 and 11 have been amended to depend from claim 75 in view of the cancellation of claims 8 and 74. This amendment is supported, for example, by claims 8 to 10 as originally filed, and in the specification, for example, on page 12, line 27, to page 13, line 2, which indicates that SEQ ID NOS:12, 24 and 25 correspond to TPBD amino acid sequences.

Claims 68 and 75 have been amended to recite SEQ ID NOS:12, 24 and 25. These amendments add no new matter.

Claims 70 and 71 have been amended to depend from claim 72, and claim 72 has been amended to depend from claim 68, in view of the cancellation of claim 69. These amendments are supported, for example, by claims 68 to 72 as originally filed.

As set forth above, the amendments are fully supported by the specification and claims as originally filed and do not introduce new matter. Accordingly, entry of the amendments is respectfully requested.

Regarding the rejection under 35 U.S.C. § 112, first paragraph

The objection to the specification and corresponding rejection of claims 69 to 71, 73 and 46 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in the specification, are respectfully traversed. Applicants respectfully submit that the specification provides sufficient description of the claimed anti-TPBD antibodies to enable claims 69 to 71 and 73, and sufficient description of the claimed therapeutic composition to enable claim 46.

Regarding claims 69 to 71 and 73, the Office Action asserts that the specification lacks description of how to design an antibody that can bind to a TPBD and increase the interaction of the TPBD with a TPBD-binding protein. Applicants submit that the specification provides guidance for making a variety of anti-TPBD antibodies, including those that increase the interaction of a TPBD with a TPBD-bindng. Using this guidance, Applicants submit that an anti-TPBD need not be "designed" but also can be identified by screening. The specification teaches assays useful for screening to identify antibodies, including, for example, bioassays for identifying compounds that modulate the activity of a TPBD (page 62, lines 15-18). Applicants submit that those skilled in the art would have used such assays to identify an antibody that can bind to a TPBD and increase the interaction of the TPBD with a TPBD-binding protein. Nevertheless, to further prosecution, claims 69 and 73 have been cancelled, and claims 70 and 71 have been amended to depend from claim 72, which recited an anti-TPBD antibody that inhibits the association of the TPBD with a TNF family receptor, TRAF protein or TRAF-associated protein.

Regarding claim 46, the Office Action asserts that the specification lacks description of how an anti-TPBD antibody could be used to contact a TPBD in the cytoplasm of a cell. Specifically, the Office Action alleges that the claimed anti-TPBD antibody would bind to the external domain of the TNF-receptor and would not be internalized, and as such, it would not be expected that the antibody would contact TPBD in the cell cytoplasm. Applicants respectfully

point out that the claimed isolated anti-TPBD antibody has specific reactivity with a TPBD amino acid sequence selected from SEQ ID NOS:12, 24 and 25. For this reason the claimed antibody would not be expected to bind to the external domain of the TNF receptor. Instead, it would be expected that the anti-TPBD antibody would bind to TPBP upon entry into the cell, for example, by internalization. Applicants submit that those skilled in the art would have been able to use a variety of methods for delivering an anti-TPBD antibody into a cell. For example, at the time of filing the present application, a variety of well-known methods were available for improving efficiency of antibody uptake via endocytosis. As evidence of the high level of skill in the art with respect to antibody internalization, Applicants wish to point out two articles published before the priority date of the subject application. Specifically, Pardridge et al. The Journal of Pharmacology and Experimental Therapeutics, 286:548-554 (1998) and Pardridge et al. Immunology Letters, 42:191-195 (1994), describes cationization of antibodies to facilitate both trans-endothelial migration and target cell endocytosis. These publications indicate that cationization greatly augments the uptake and endocytosis of a monoclonal antibody and a humanized monoclonal antibody. Finally, in contrast to the assertion in the Office Action that work with clinical specimens would be required to ensure selection of an antibody that has the specificity necessary for binding to a TPBD, Applicants submit that the specification teaches assays useful for confirming antibody specificity that would have been used by those skilled in the art to assess the clinical usefulness of a given antibody (see, for example, the Examples section). Nevertheless, to further prosecution, claim 46 has been cancelled herein without prejudice to Applicants pursuit of this claim in a related application that claims the benefit of priority to the subject application.

As indicated above, this rejection has been rendered moot with respect to claims 46, 69 and 73, which has been cancelled, and with respect to claims 70 and 71, which have been amended to depend from claim 72. Accordingly, Applicants respectfully request removal of this rejection under 35 U.S.C. § 112, first paragraph.

Regarding the rejection under 35 U.S.C. § 102(b)

The rejection of claims 8, 11, 46, 68 to 72, 74 to 76, 83 and 86 under U.S.C. § 102(b) as allegedly anticipated by Everett et al. The EMBO Journal 16:1519-1530 (1997) is respectfully traversed. Applicants respectfully submit that the isolated anti-TPBD antibodies of claims 9, 11, 68, 70 to 72, 75 and 83, as amended, are novel over the cited reference. This rejection has been rendered moot with respect to claims 11, 46, 74, 76 and 86, which have been cancelled herein.

The Office Action states that Everett et al. describes a polyclonal serum, r29, raised against HAUSP residues 28 to 427. As amended, claims 9, 11, 68, 70 to 72, 75 and 83 are directed to isolated antibodies having specific reactivity with TRAF7 (SEQ ID NO:12), the TRAF domain of TRAF7 (SEQ ID NO:25) or the TRAF domain of SPOP (SEQ ID NO:24). Applicants submit that Everett et al. lacks description of antibodies having specific reactivity with a polypeptide corresponding to any of the recited amino acid sequences. Therefore, claims 9, 11, 68, 70 to 72, 75 and 83 are novel over the cited reference. Accordingly, Applicants respectfully request removal of this rejection under U.S.C. § 102(b).

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned agent or Cathryn Campbell.

Respectfully submitted,

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